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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,725	02/06/2002	Wayne Kindsvogel	01-04	8714

7590 07/20/2006

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,725	KINDSVOGEL, WAYNE	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 April 2006 has been entered.

2. Claims 9 and 11-24 are canceled.

Claims 1 and 10 have been amended.

Claims 25-29 have been added.

3. Claims 1-8, 10 and 25-29 are pending and under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Rejections Withdrawn

6. The rejection of claims 1-8 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter into the claims is withdrawn in view of the amendments to the claims.

New Grounds of Objections/Rejections

7. Claims 1-8, 10 and 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation "at an eptiope within a polypeptide consisting of at least one of amino acids..." in claim 1 as it is unclear whether the polypeptide and epitope consists of just a few of amino acids 30 to 67 of SEQ ID NO:4 (i.e., "at least one of amino acids...") and just a few of amino acids 68 to 154 of SEQ ID NO:4, i.e., combinations of amino acids taken from resideus 30 to 67 and 68 to 154 of SEQ ID NO:4 or does the TACI polypeptide consist of amino acids 30 to 67 and 68 to 154 of SEQ ID NO:4 or does the phrase refer to the TACI polypeptide of SEQ ID NO:4 wherein the anitbody component binds at an epiotpe within amino acids 30 to 67 of SEQ ID NO:4 or within amino acids 68 to 154 of SEQ ID NO:4? Further, in view of dependent claims 10 and 25-29 does the TACI polypetide consist only of amino acids 110 to 118, 30 to 67, 68 to 154, 39 to 50, 78 to 91 of SEQ ID NO:4 as written or does the antibody component bind within amino acid residues 110 to 118, 30 to 67, 68 to 154, 39 to 50 or 78 to 91 of SEQ ID NO:4?

8. Claims 1-8, 10, and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The amendments to the claims filed 2/27/2006 have introduced new matter. As presently amended claim 1 recites "wherein binding to TACI is at an epitope wihtin a polypeptide consisting of at least one of amino acids 30 to 67 of SEQ ID NO:4 and amino acids 68 to 154 of SEQ ID NO:4". There is insufficient written support for targeting tumor cells with an antibody component that binds BCMA and TACI wherein the antibody component binds TACI at an epitope within a polypeptide consisting of at least one of amino acids 30 to 67 and amino acids 68 to 154 of SEQ ID NO:4, which encompasses amino acids from both extracellular fragments of TACI (i.e., amino acids 30 to 67 and 68 to 154 of SEQ ID NO:4). The as filed disclsoure as pointed to by applicant appears to provide adequate written support for monoclonal antibodies that bind both BCMA and TACI wherein binding to BCMA is within a region consisting of amino acids 13 to 27 of SEQ ID NO:2 and wherein binding to TACI is at an epitope within amino acids 30 to 67 of SEQ ID NO:4 or within amino acids 68 to 154 of SEQ ID NO:4, i.e., two fragments of the TACI extracellular domain (see top of pg. 4 of the specification). Further, at pg. 3, the specification disclsoes that murine monoclonal antibodies were prepared against a fragment of the BCMA extracellular domain and was unexpectaedly found to also bind TACI within the above residues of the TACI extracellular domain. Thus, the disclosure does not provide sufficient guidance and direction to the presently claimed method encompassing administering an antibodies raised against just any BCMA peptide or polypeptide that would cross-react with amino

acids 30-67 and 68-154 of the TACI extracellular domain, in view that such a finding was unexpected. The binding of the monoclonal antibody to both BCMA and TACI is disclosed as binding to the extracellular domain of BCMA represented by residues 13-27 of SEQ ID NO:2 and the monoclonal antibody is disclosed to also bind two fragments of the TACI extracellular domain, represented by residues 30 to 67 of SEQ ID NO:4 and 68 to 154 of SEQ ID NO:4 (top of pg. 4 of specification). Thus, there is insufficient written support for the claimed antibodies that bind both BCMA and TACI wherein binding to TACI is at an epitope within amino acids 30-67 and 68-154 of SEQ ID NO:4 or at an epitope that spans amino acids 30 to 67 and 68 to 154 of SEQ ID NO:4 (i.e., "at least one of amino acids 30 to 67 of SEQ ID NO:4 and amino acids 68 to 154 of SEQ ID NO:4") as presently recited. Amending claim 1 to recite that the composition comprises a monoclonal antibody that binds to both BCMA and TACI and "wherein the binding to BCMA is within amino acids 13 to 27 of SEQ ID NO:2 and wherein binding to TACI is at an epitope within amino acids 30 to 67 and 68 to 154 of the polypeptide of SEQ ID NO:4." or similar language would overcome the above new matter rejection. Similarly, dependent claims 10 and 25-29 should also be amended to recite "wherein the monoclonal antibody binds to an epitope within amino acid residues X to Y of SEQ ID NO:4", consistent with base claim 1.

Additionally, there does not appear to be adequate written support for newly presented claims 28-29, which recite wherein the binding to TACI is at an eptiope within a polypeptide consisting of amino acids 39 to 50 of SEQ ID NO:4 or consisting of amino acids 78 to 91 of SEQ ID NO:4. The as filed disclsoure at pg. 4, lines 22-26 discloses

that the anti-BCMA-TACI antibody components can bind a polypeptide having the amino acid sequence of amino acids 39 to 50 of SEQ ID NO:4 or a polypeptide having the amino acid sequence of amino acids 78 to 91 of SEQ ID NO:4. Thus, in view of the transitional term "having", which is equivalent to "comprising" in light of the specification (MPEP 2111.03), the disclsoure is not limited to antibodies specific to the recited epiotpes within amino acids 39 to 50 of SEQ ID NO:4 or within amino acids 78 to 91 of SEQ ID NO:4. The claims recite that the polypeptide consists of ("consisting of" being closed claim language; MPEP 2111.03) amino acids 39 to 50 of SEQ ID NO:4 or the polypeptide consists of amino acid residues 78 to 91 of SEQ ID NO:4. Thus, there is insufficient written support for the narrower limitations of the present claims, i.e., consisting of amino acids 39 to 50 of SEQ ID NO:4 and consisting of amino acids 78 to 91 of SEQ ID NO:4. While it is acknowledged that the recited TACI regions of claims 28-29 are within the broader TACI extracellular regions of amino acids 30 to 67 and 68 to 154 of SEQ ID NO:4, applicant is remidned that it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Applicant is required to provide sufficient written support for the limitations recited in newly added claims 28-29 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-8 and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Theill et al (US Patent 6,774,106 B2, priority to 5/12/2000) in view of Gross et al (WO 00/40716, 7/13/2000).

The claims are drawn to a method for inhibiting the proliferation of tumor cells comprising endogenous BCMA or TAC or both, comprising administering a composition or pharmaceutical composition comprising an antibody component that binds both BCMA and TACI wherein binding to TACI is at an epitope within amino acids 30-67 or 68-154 of SEQ ID NO:4, wherein the BCMA-TACI is a naked antibody or antibody fragment or is conjugated to a therapeutic agent or cytotoxic agent or wherein the BCMA-TACI antibody component binds the recited epitopes of claims 26-29.

Theill et al teach a method of treating cancer comprising administering a composition comprising an antagonistic antibody or antigen-binding fragment thereof (i.e., naked antibodies) that bind both BCMA and TACI (see entire document, particularly columns 11-17). Further, Theill et al teach that ligand binding to the cell surface receptors BCMA and TACI on T and B cell lymphomas results in the stimulation of proliferation of B and T cells in vitro and in vivo. Theill et al do not specifically teach wherein binding to TACI is within the recited amino acid epitopes or wherein the BCMA-TACI antibody component is conjugated to the recited therapeutic moieties or a cytotoxic polypeptide and pharmaceutical composition comprising the BCMA-TACI antibody component. These deficiencies are made up for in the teachings of Gross et al.

Gross et al teach methods of inhibiting the ligand binding activity of TACI for the treatment of B-cell cancers comprising administering an antibody that binds to the cytsteine-rich pseudo repeat of TACI (SEQ ID NO:10), and which is the ligand binding site of TACI and Gross et al teach antibody conjugates comprising various therapeutic and diagnostic agents, including cytotoxic polypeptides and pharmaceutical compositions comprising the antagonistic antibody (see entire document, particularly pp. 2, pg. 3, lines 29-37, pg 54, 56, lines 21-24, pp. 72-73, 83-84).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method for inhibiting tumor cell proliferation comprising administering a composition or pharmaceutical composition comprising an antibody that binds BCMA and TACI, wherein binding to TACI is within

the cysteine rich domains and the BCMA-TACI antibody is conjugated to a therapeutic or diagnostic agent for therapeutic benefit in lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a method for inhibiting tumor cell proliferation comprising administering a composition or pharmaceutical composition comprising an antibody that binds BCMA and TACI, wherein binding to TACI is within the cysteine rich domains and the BCMA-TACI antibody is conjugated to a therapeutic or diagnostic agent for therapeutic benefit in lymphoma patients in view of Theill et al and Gross et al because Theill et al teach a method of treating cancer comprising administering a composition comprising an antibody that binds both BCMA and TACI and antagonizes the receptors and Gross et al teach methods of inhibiting the ligand binding activity of TACI for the treatment of B-cell cancers (i.e., lymphomas and leukemias) comprising administering an antibody that binds to the cytsteine-rich pseudo repeat of TACI (SEQ ID NO:10), which is the ligand binding site of TACI and Gross et al teach antibody conjugates comprising various therapeutic and diagnostic agents, including cytotoxic polypeptides and pharmaceutical compositions comprising the antagonistic antibody. Therefore, one of ordinary skill in the art would have been motivated with a reasonable expectation of success to modify the BCMA-TACI specific antibodies of Theill et al to bind the cysteine-rich domains of TACI, the known ligand binding regions of TACI in order to antagonize ligand binding where receptor-ligand engagement is associated with B cell proliferation in lymphomas. Thus, the TACI specificity of the antibody that binds both BCMA and TACI would

necessarily bind the recited epitopes of TACI (SEQ ID NO:4), inclusive to the TACI cysteine-rich domains. Further, one of ordinary skill in the art would have been motivated to conjugate the BCMA-TACI antibody to the known diagnostic and cytotoxic therapeutic agents and produce a pharmaceutical composition comprising the BCMA-TACI antibody as taught by Gross et al for therapy in lymphoma patients with a reasonable expectation of success. Thus, it would have been *prima facie* obvious to one skilled in the art to have produced a method for inhibiting tumor cell proliferation comprising administering a composition or pharmaceutical composition comprising an antibody that binds BCMA and TACI, wherein binding to TACI is within the cysteine rich domains and the BCMA-TACI antibody is conjugated to a therapeutic or diagnostic agent for therapeutic benefit in lymphoma patients in view of Theill et al and Gross et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at

(571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827